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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/767,561	01/28/2004	Gordon J. Freeman	WYS-01804	5098

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EXAMINER	
GAMBEL, PHILLIP	

ART UNIT	PAPER NUMBER
1644	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/767,561	FREEMAN ET AL.	
	Examiner	Art Unit	
	Phillip Gambel	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 August 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office Action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission, filed on 08/18/2008, has been entered.

Applicant's amendment, filed 08/08/2008, has been entered.

Claims 1-3 have been amended.

Claims 1-14 are pending.

2. The text of those sections of Title 35 USC not included in this Action can be found in a prior Office Action.

This Action will be in response to applicant's arguments, filed 08/08/2008.

The rejections of record can be found in the previous Office Actions, mailed 02/07/2007 and 10/19/2007.

3. Advisory Action.

Applicant's Remarks, filed 08/08/2008, concerning the Advisory Action, mailed 03/17/2008, are acknowledged and will be addressed as they read on the entered amendment, including amended claims, filed with RCE.

4. Acknowledgement of Species Election.

The examiner acknowledges applicant provisionally elected the species "B7-2 encoding nucleic acids without additional molecules" and "sarcoma" for search purposes only, in the Response to Restriction Requirement mailed on November 6, 2006, filed 11/09/2006.

The examiner's previous indication that applicant elected the species "anti-inflammatory agents, and aspirin as the ultimate species in the Reply to Restriction Requirement, filed on 2/15/06" was inadvertent.

The examiner apologizes for any inconvenience or confusion to applicant in this matter.

5. Incorporation by Reference.

Applicant's amendment, including amending the claims and the specification via reliance upon the incorporation by reference to U.S. serial number 08/109,393, to which the present application claims priority (applicant notes thatthe entire contents of which were incorporated by reference on page 1, lines 10-11 of the instant application and that no new matter has been added) is acknowledged.

6. This is a 35 U.S.C § 112, first paragraph, "written description" (and not new matter).

Claims 1-3 and 6-14 are rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed.

Applicant's amended claims, filed 08/18/2008, now recite:
"a) at least 100 contiguous amino acids of SEQ ID NO: 2 or 4; or
b) a polypeptide that is at least 50% homologous to SEQ ID NO: 2 or 4".

There is insufficient written description of the genus set forth in instant claims and dependent claims thereof, which now recite:
a) at least 100 contiguous amino acids of SEQ ID NO: 2 or 4; or
b) a polypeptide that is at least 50% homologous to SEQ ID NO: 2 or 4".
in the context of "nucleic acid molecules encoding B7-2 molecules and fragments thereof, which have the ability to costimulate a T cell and the ability to bind a CD28 or CTLA4", broadly encompassed by the claimed invention.

Even though the current claims now recite "at least 100 contiguous amino acids of SEQ ID NO: 2 or 4" rather than at least 20 contiguous amino acids of SEQ ID NO: 2 or 4";
applicant's arguments, filed 08/08/2008, have been fully considered but have not been found convincing essentially for the reasons of record.

The recitation of "a polypeptide that is at least 50% homologous to SEQ ID NO: 2 or 4" remains the same upon the filing of the RCE.

Applicant argues in conjunction with certain legal decisions as well as material incorporated by reference from USSN 08/280,757 (now U.S. Patent No. 6,130,316)
that the claims recite d particular chemical structures (e.g., SEQ ID NOS. 2/4) and
that the specification and priority documents are replete with teachings of the functional characteristics of the molecules encoded by the nucleic acids use in the claimed methods (e.g., "ability to costimulate a T cell and the ability to bind a CD28 or CTLA4 ligand");
thereby providing for a clear teachings of the structural and functional characteristics of the claimed nucleic acids.

Applicant also asserts that a correlation between chemical structure and function via using the chemical structure and function of human B7-2 to isolate and characterize murine B7-2 (e.g., see Example 6) to provide for the sufficiency of the instant (and priority) disclosure(s).

Applicant assert that a person of ordinary skill in the would readily recognize that methods that are essentially identical to those used in Examnple 6 could also be used to isolate other B7-2 species, and, hence, the claimed methods fall well-within the scope of the written description provided in the specification.

In responding to the legal citations noted in the previous rejections of record,
applicant notes
that applicant has taught a representative number of species having the structure and properties of the B7-2 nucleic acids as well as detailed methods for the isolation of other B7-2 encoding nucleic acids of the claimed methods and
that applicant has provided a level of written description far exceeding "a potential method for isolating" the claimed B7-2 molecules.

In addressing the five references supporting the rejection of record (e.g., Riley et al., Coyle et al., Metzler et al., Attwood, Skolnick et al.),
applicant asserts distinguishing features that would indicate that these reference do not provide a preponderance of the evidence that a person of skilled in the art would recognize in an applicant's disclosure a description of the invention defined by the claims (e.g., see MPEP 2163.04).

However, the examiner maintains that the prior rejection, including the evidentiary references, is applicable to the claimed invention.

It is noted that applicant's Examples rely upon cloning and sequencing B7-2 from a murine B cell tumor line (activated M12; see Example 6) as well as cloning and sequencing B7-2 from human splenic B cells.

Therefore, applicant has relied upon isolating and cloning two species of B7-2 from cells that express B7-2.

While applicant relies upon the disclosure of certain structural characterization (e.g. sequences), of isolating variants of these two species, based in-part upon functional characteristics (e.g., "ability to stimulate a T cell and to bind a CD28 or CTLA4 ligand");
Applicant has not provided objective evidence of to other variants encompassed by the claimed invention that meets the claimed B7-2 molecules employed in the claimed methods.

For example, although applicant's assertions rely upon a degree of homology to support the written description of the instant claims (e.g., "a polypeptide that is at least 50% homologous to SEQ ID NOS 2 / 4") to distinguish the instant claims from previous legal holdings,
the degree of variability of the claimed B7-2 molecules in the instant invention is still large.

As indicated previously with respect to applicant's reliance upon various screening assays, the Court has held that the disclosure of screening assays and general classes of compounds was not adequate to describe compounds having the desired activity: without disclosure of which peptides, polynucleotides, or small organic molecules have the desired characteristic, the claims failed to meet the description requirement of § 112. See University of Rochester v. G.D. Searle & Co., Inc., 69 USPQ2d 1886,1895 (Fed. Cir. 2004).

Again as noted previously, the problem here is that the instant specification fails to provide a disclosure of which residues are required for the B7-2 molecule and fragments thereof that would retain the ability to costimulate a T cell and the ability to bind a CD28 or CTLA4 in B7-2 molecules and fragments thereof, other than the those B7-2 molecules isolated and cloned from a murine B cell tumor line M12 or from human anti-IgM activated B cells.

The examiner maintains the evidentiary references of record do support sufficient concerns about variation in structure and function with respect to costimulatory molecules to indicate that applicant was not in possession of the relevant identifying characteristics such as the structure of other physical and/or chemical characteristics of the claimed genus of B7-2 molecules and fragments thereof, indicating a lack of compliance with the Written Description guidelines.

A skilled artisan cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus that exhibit this functional property.

Therefore, there is insufficient written description for genus of "B7-2 molecules comprising a limited sequence of nucleic acids encoding 100 amino acids or having 50% homology" to essentially two (2) examples of functional B7-2 molecules isolated and cloned from a murine and human cells, broadly encompassed by the claimed invention at the time the invention was made and as disclosed in the specification as filed under the written description provision of 35 USC 112, first paragraph.

The following of record is reiterated for applicant's convenience.

There is insufficient written description of the claimed genus of "B7-2 molecules" or "B7-2 molecules having the ability to costimulate a T cell and the ability to bind a CD28 or CTLA4" wherein the nucleic acids encode
a) at least 100 contiguous amino acids of SEQ ID NO: 2 or 4; or
b) a polypeptide that is at least 50% homologous to SEQ ID NO: 2 or 4".
in the absence of defining the relevant identifying characteristics such as the structure of other physical and/or chemical characteristics of the claimed genus and, in turn, there is insufficient written description of such identifying characteristics of the claimed genus of "B7-2 molecules and fragments thereof having the ability to costimulate a T cell and the ability to bind a CD28 or CTLA4" in the specification as-filed, commensurate in scope with the claimed invention.

For example, there is insufficient structural information or defining characteristics, which provide for a sufficient written description of the "B7-2 molecules and fragments thereof", as broadly claimed.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, 1116 (Fed. Cir. 1991). makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016 (Fed. Cir. 1991).

One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481, 1483. In Fiddes v. Baird, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence. Thus, the specification fails to describe these DNA sequences. The Court further elaborated that generic statements are not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. Finally, the Court indicated that while applicants are not required to disclose every species encompassed within a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, defined by nucleotide sequence, falling within the scope of the genus. See The Regents of the University of California v. Eli Lilly and Company, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

For example, the instant specification discloses specific species of murine and human B7-2 molecules and does not provide a sufficient number of species that support the claimed genus of "B7-2 molecules and fragments thereof having the ability to costimulate a T cell and the ability to bind a CD28 or CTLA4".

Applicant is relying upon certain biological activities and the disclosure of a limited number of species to support entire genera. Yet, the instant specification does not provide sufficient written description as to the structural features of said "B7-2 molecules and fragments thereof", as currently encompassed by the instant claims.

Also, the specification does not provide for a sufficient correlation between the chemical structure and the function of the genus of "B7-2 molecules and fragments thereof", currently encompassed by the claimed invention. The reliance on the disclosed limited examples of specific human and murine B7-2 molecules that meet the claimed "B7-2 molecules and fragments thereof" indicated above and disclosed in the specification as filed does not support the written description of any "B7-2 molecules and fragments thereof" broadly encompassed by the instant claims. It has been well known that minor structural differences even among structurally related compounds or compositions can result in substantially different biology, expression and activities. The specification as filed does not provide written description for "B7-2 molecules and fragments thereof", commensurate in scope with the claimed invention.

There is insufficient written description to lead a person of skill in the art to know which sequences are essential, which sequences are non-essential, and what particular sequence lengths identify essential sequences for identifying "B7-2 molecules and fragments thereof having the ability to costimulate a T cell and the ability to bind a CD28 or CTLA4".

A person of skill in the art was not in possession of the breadth of claimed "B7-2 molecules and fragments thereof" because it was well known in the art at the time the invention was made that different molecules having sequence similarity to costimulatory molecules such as B7-1 and B7-2 have different, and often opposite, functions (e.g. reviewed by Riley et al., 2005, Blood, 105: 13 - 21; see entire document).

Also, Coyle et al. (Nature Immunology 2: 203-209, 2001) disclose that B7-1 and B7-2 exhibit pronounced differences in structural and functional characteristics (page 204, column 1; The B7-1 and B7-2 Family) and disclose the increasing complexity in costimulatory signal regulating T cell function, wherein a number of molecules are poorly understood and likely have distinct roles in regulation T cells (see entire document).

Further, even single amino acid differences can result in drastically altered functions between two costimulatory proteins. For example, Metzler et al. (Nature Structural Biol. 1997; 4:527-531) show that any of a variety of single amino acid changes can alter or abolish the ability of CTLA4 to interact with its ligands CD80 and CD86 (e.g., summarized in Table 2). Thus, one would not expect possession of the scope of the claimed genera by relying on functional activities that will be shared by two polypeptides having less than 100% identity over the full length of their sequences.

Attwood (Science 290: 471-473, 2000) teaches that "[i]t is presumptuous to make functional assignments merely on the basis of some degree of similarity between sequences.

Similarly, Skolnick et al. (Trends in Biotech. 18: 34-39, 2000) teach that the skilled artisan is well aware that assigning functional activities for any particular protein or protein family based upon sequence homology is inaccurate, in part because of the multifunctional nature of proteins (e.g., "Abstract" and "Sequence-based approaches to function prediction", page 34). Even in situations where there is some confidence of a similar overall structure between two proteins, only experimental research can confirm the artisan's best guess as to the function of the structurally related protein (see in particular "Abstract" and Box 2).

Mere idea or function is insufficient for written description; isolation and characterization at a minimum are required

The instant claims do not provide sufficient structural and functional characteristics coupled with a known or disclosed correlation between function and structure. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus of "B7-2 molecules and fragments thereof".

The Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, 1 "Written Description" Requirement makes clear that if a claimed genus does not show actual reduction to practice for a representative number of species; then the Requirement may be alternatively met by reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, see especially page 1106 column 3).

In the absence of structural characteristics that are shared by members of the genus of "B7-2 molecules and fragments thereof having the ability to costimulate a T cell and the ability to bind a CD28 or CTLA4",
the skilled artisan would conclude that the disclosure fails to provide a representative number of species to describe the genus.

Thus, Applicant was not in possession of the claimed genus. See University of California v. Eli Lilly and Co. 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997).
Also, see MPEP 2163.
"Adequate written description requires a precise definition, such as by structure, formula, chemical name or physical properties, not a mere wish or plan for obtaining the claimed chemical invention." Id. at 1566, 43 USPQ2d at 1404 (quoting Fiers, 984 F.2d at 1171, 25 USPQ2d at 1606). Also see Enzo-Biochem v. Gen-Probe 01-1230 (CAFC 2002).

Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

Applicant's arguments have not been found persuasive.

Applicant is invited to limit the invention to the disclosed human and mouse "B7-2 molecules" to obviate this rejection.

7. Claims 1-3 and 6-14 are rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for certain nucleic acids encoding certain murine and human B7-2 encoding nucleic acids encoding the first peptide set forth in the claimed B7-2 fusion protein encoding nucleic acid and while being enabling for reliance upon known immunoglobulin constant regions for nucleic acids encoding the second peptide set forth in the claimed B7-2 fusion protein molecules as disclosed in the specification as filed, does not reasonably provide enablement for any

"B7-2 molecule and fragments thereof having the ability to costimulate a T cell and the ability to bind a CD28 or CTLA4"

"wherein the nucleic acid molecule encodes

a) at least 100 contiguous amino acids of SEQ ID NO: 2 or 4; or

b) a polypeptide that is at least 50% homologous to SEQ ID NO: 2 or 4".

The specification does not enable any person skilled in the art to which it pertains, or with which it is most clearly connected, to make and use the invention commensurate in scope with these claims.

Applicant's arguments, filed 08/18/2008, have been fully considered but have not been found convincing essentially for the reasons of record.

Even though the current claims now recite "at least 100 contiguous amino acids of SEQ ID NO: 2 or 4" rather than at least 20 contiguous amino acids of SEQ ID NO: 2 or 4";

applicant's arguments, filed 08/08/2008, have been fully considered but have not been found convincing essentially for the reasons of record.

The recitation of "a polypeptide that is at least 50% homologous to SEQ ID NO: 2 or 4" remains the same upon the filing of the RCE.

Applicant argues the following.

Applicants respectfully traverse the rejection. As discussed above, Example 6 contains ample guidance that would steer the skilled artisan toward B7-2 molecules with the claimed sequence homology and functional properties. This is not a prophetic example, Applicants have demonstrated that this method actually works. A person of ordinary skill in the art would readily recognize that the method could be used to isolate nucleic acids encoding other B7-2 molecules. Therefore, the degree of enablement provided by the Applicants is not merely limited to "a starting point from which one of skill in the art can perform studies with the known B7-2 molecules to practice the claimed invention" (emphasis in original; page 10, paragraph 3 of the instant Office Action). As discussed supra, Applicants have clearly enabled methods that would clearly lead to the isolation of other B7-2 molecular species. The Examiner then proceeds to cite the same journal articles cited in the foregoing rejection under 35 U.S.C. § 112, first paragraph (written description), to allegedly demonstrate that Applicants have not provided an enabling disclosure of the recited nucleic acid molecules.

Applicants respectfully incorporate by reference the arguments advanced above.

As acknowledged by applicant's arguments, the arguments and rebuttal with respect to the instant claims as they applied to the written description rejection above to the enablement rejection herein.

Therefore, applicant argues in conjunction with certain legal decisions as well as material incorporated by reference from USSN 08/280,757 (now U.S. Patent No. 6,130,316)
that the claims recite d particular chemical structures (e.g., SEQ ID NOS. 2/4) and
that the specification and priority documents are replete with teachings of the functional characteristics of the molecules encoded by the nucleic acids use in the claimed methods (e.g., "ability to costimulate a T cell and the ability to bind a CD28 or CTLA4 ligand");
thereby providing for a clear teachings of the structural and functional characteristics of the claimed nucleic acids.
Applicant also asserts that a correlation between chemical structure and function via using the chemical structure and function of human B7-2 to isolate and characterize murine B7-2 (e.g., see Example 6) to provide for the sufficiency of the instant (and priority) disclosure(s).

Applicant assert that a person of ordinary skill in the would readily recognize that methods that are essentially identical to those used in Example 6 could also be used to isolate other B7-2 species, and, hence, the claimed methods fall well-within the scope of the enablement (vs. written description) provided in the specification.

In responding to the legal citations noted in the previous rejections of record,
applicant notes
that applicant has taught a representative number of species having the structure and properties of the B7-2 nucleic acids as well as detailed methods for the isolation of other B7-2 encoding nucleic acids of the claimed methods and
that applicant has provided a level of enabling disclosure (vs. written description) far exceeding "a potential method for isolating" the claimed B7-2 molecules.

In addressing the five references supporting the rejection of record (e.g., Riley et al., Coyle et al., Metzler et al., Attwood, Skolnick et al.),
applicant asserts distinguishing features that would indicate that these reference do not provide a preponderance of the evidence that a person of skilled in the art would recognize in an applicant's disclosure (an enabling disclosure (vs. a description) of the invention defined by the claims.

However, the examiner maintains that the prior rejection, including the evidentiary references, is applicable to the claimed invention.

It is noted that applicant's Examples rely upon cloning and sequencing B7-2 from a murine B cell tumor line (activated M12; see Example 6) as well as cloning and sequencing B7-2 from human splenic B cells.

Therefore, applicant has relied upon isolating and cloning two species of B7-2 from cells that express B7-2.

While applicant relies upon the disclosure of certain structural characterization (e.g. sequences), of isolating variants of these two species, based in-part upon functional characteristics (e.g., "ability to stimulate a T cell and to bind a CD28 or CTLA4 ligand");
applicant has not provided objective evidence of to other variants as encompassed by the claimed invention that meets the claimed B7-2 molecules employed in the claimed methods.

For example, although applicant's assertions rely upon a degree of homology to support the written description of the instant claims (e.g., "a polypeptide that is at least 50% homologous to SEQ ID NOS 2 / 4") to distinguish the instant claims from previous legal holdings,
the degree of variability of the claimed B7-2 molecules in the instant invention is still large.

As indicated previously, with regard to the amended claims indicated above, applicant relies pages 11-12 of the instant specification; pages 4 and 14-15 of USSN 08/190,393; and Example 7 of U.S. Patent No. 6,130,316 for support for nucleic acid molecules encoding fragments of B7-2. In addition, applicant relies upon page 3 and 13 of USSN 08/109,393 and SEQ ID NOS. 2 and 4 for the support of the percent claimed percent homology and notes that SEQ ID NOS 2 and 4 are themselves 50% homologous with each other.

In contrast to the references cited in support of the rejection of record,
applicant asserts that ample guidance as to how one skilled in art would make and use the claimed invention, including guidance for ex vivo modification of tumor cells and the type of tumor cells that may be modified with respect to the claimed genus of B7-2 molecules and fragments thereof in compliance with the enablement requirement of 35 USC 112, first paragraph.

In contrast to applicant's assertions, the instant specification does not provide sufficient guidance that would steer the skilled artisan towards those "B7-2 molecules and fragments thereof, particularly as to those nucleic acid / amino sequences with limited sequence or sequence homology responsible for retaining the ability to costimulate a T cell and the ability to bind a CD28 or CTLA4" that could be used to carry out the claimed methods – an essentially element of the every claim of the instant application – and has not provided sufficient evidence that such modifications were within the knowledge of the skilled or ordinary artisan at the time the invention was made.

Therefore, the amount of direction or guidance presented and the number of working examples provided in the specification as filed was narrowly limited to the known B7-2 molecules isolated and cloned from a murine B cell tumor line M12 or from human anti-IgM activated B cells.

What is missing from the specification as filed is the disclosure of sufficient direction or examples of how to modify tumor cells with nucleic acids encoding B7-2 molecules and fragments thereof relying upon limited sequences or sequence homology, other than the known murine and human B7-2 molecules.

In contrast to applicant's assertions including the provision of specific starting materials and the conditions under which a process is to be carried out,

the screening assays provide a starting point from which one of skill in the art can perform studies with the known B7-2 molecules to practice the claimed invention, but this is not adequate to constitute enablement in that will enable any person skilled in the art to make and use the invention as it reads on ill-defined modifications to these previously isolated and functional B7-2 molecules,

wherein the costimulatory molecules including the B7 antigens such as B7-2 exhibit pronounced differences in structural and functional characteristics.

Again, in contrast to applicant's assertions,

the examiner maintains the evidentiary references of record do support sufficient concerns about variation in structure and function with respect to costimulatory molecules to indicate that applicant was not enabled for the full breadth of the claimed invention.

See Coyle et al., Nature Immunology 2: 203-209, 2001; Metzler et al., Nature Structural Biol. 4:527-531, 1997; and Riley et al., Blood, 105: 13 – 21, 2005 cited of record and reiterated herein in the rejection under 35 USC 112, first paragraph, enablement.

One skilled in the art would not know the identity of any non-disclosed modifications to the known B7-2 molecules falling within the scope of the claim and consequently would not be able to make said non-disclosed B7-2 molecules and fragments thereof and use said non-disclosed B7-2 molecules and fragments thereof in the modification of tumor cells, broadly encompassed by the claimed invention.

Assays for investigating a known products is not equivalent for making and using ill-defined modifications.

If the skilled artisan cannot make the product, then the skilled artisan cannot use the product.

There is insufficient nexus to the specification and the claimed methods, which rely upon a genus of B7-2 molecules and fragments thereof.

In contrast to applicant's assertions, the instant specification does not provide sufficient guidance that would steer the skilled artisan towards modifications to B7-2 molecules and fragments thereof which the B7-2 molecules and fragments thereof would retaining the ability to costimulate a T cell and the ability to bind a CD28 or CTLA4 that could be used to carry out the claimed methods

Therefore, the amount of direction or guidance presented and the number of working examples provided in the specification as filed was narrowly limited to the known murine and human B7-2 isolated from B cells or B tumor cells.

"A recurring problem is whether a specification that sets forth a single or a limited number of examples can be enabling of broad claims when the subject matter concerns biological materials or reactions which are generally considered to be unpredictable."

See Enzo Biochem Inc. v. Calgene Inc. 52 USPQ2d 1129, 1138 (CAFC 1999).

Given the relative incomplete understanding in the biotechnological field involved, and the lack of a reasonable correlation between the narrow disclosure in the specification and the broad scope of protection sought in the claims, a rejection under 35 USC 112, first paragraph for lack of enablement is deemed appropriate.
See MPEP 2164.08.

A patent is granted for a completed invention, not the general suggestion of an idea and how that idea might be developed into the claimed invention. In the decision of Genentech, Inc, v. Novo Nordisk, 42 USPQ 2d 100,(CAFC 1997), the Court held that:
"[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable" and that "[t]ossing out the mere germ of an idea does not constitute enabling disclosure". The court further stated that "when there is no disclosure of any specific starting material or of any of the conditions under which a process is to be carried out, undue experimentation is required; there is a failure to meet the enablement requirements that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art", "[I]t is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement".

In contrast to appellant's assertions, the instant specification does not provide sufficient direction on how to make and use B7-2 molecules and fragments thereof as currently recited other than the isolated and functional B7-2 molecules relied upon the disclosure of the instant application as filed.

Without sufficient guidance, making and using "B7-2 molecules and fragments thereof which rely upon limited sequences or percent homology", other than limiting the "B7-2 molecules and fragments thereof to the known functional murine and human B7-2 molecules as disclosed and as defined in the specification as filed, would have been unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue.

The following is reiterated for applicant's convenience.

Reasonable correlation must exist between the scope of the claims and scope of enablement set forth.

The specification does not describe nor enable any "B7-2 molecule or fragment thereof having the ability to costimulate a T cell and the ability to bind a CD28 or CTLA4", as broadly encompassed by the claimed invention.

A person of skill in the art was not enabled to make and use the breadth of claimed "B7-2 molecule and fragment thereof" because it was well known in the art at the time the invention was made that different molecules having sequence similarity to costimulatory molecules such as B7-1 and B7-2 have different, and often opposite, functions (e.g. reviewed by Riley et al., 2005, Blood, 105: 13 - 21; see entire document).

Also, Coyle et al. (Nature Immunology 2: 203-209, 2001) disclose that B7-1 and B7-2 exhibit pronounced differences in structural and functional characteristics (page 204, column 1; The B7-1 and B7-2 Family) and disclose the increasing complexity in costimulatory signal regulating T cell function, wherein a number of molecules are poorly understood and likely have distinct roles in regulation T cells (see entire document).

Further, even single amino acid differences can result in drastically altered functions between two costimulatory proteins. For example, Metzler et al. (Nature Structural Biol. 1997; 4:527-531) show that any of a variety of single amino acid changes can alter or abolish the ability of CTLA4 to interact with its ligands CD80 and CD86 (e.g., summarized in Table 2). Thus, one would not expect the ordinary artisan to make and use the scope of the claimed genera by relying on functional activities that will be shared by two polypeptides having less than 100% identity over the full length of their sequences.

Attwood (Science 290: 471-473, 2000) teaches that "[i]t is presumptuous to make functional assignments merely on the basis of some degree of similarity between sequences.

Similarly, Skolnick et al. (Trends in Biotech. 18: 34-39, 2000) teach that the skilled artisan is well aware that assigning functional activities for any particular protein or protein family based upon sequence homology is inaccurate, in part because of the multifunctional nature of proteins (e.g., "Abstract" and "Sequence-based approaches to function prediction", page 34). Even in situations where there is some confidence of a similar overall structure between two proteins, only experimental research can confirm the artisan's best guess as to the function of the structurally related protein (see in particular "Abstract" and Box 2).

The instant claims do not provide sufficient structural and functional characteristics coupled with a known or disclosed correlation between function and structure. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus of "B7-2 molecules and fragments thereofhaving the ability to costimulate a T cell and the ability to bind a CD28 or CTLA4",
the skilled artisan would not have sufficient guidance and direction as to how to make and use the claimed "B7-2 molecules and fragments" as broadly claimed. For example, it has been well known that minor structural differences even among structurally related compounds or compositions can result in substantially different biology, expression and activities.

Further, applicant is relying upon certain biological activities and the disclosure of specific murine and human species of "B7-2 molecules" to support the genus of the claimed "B7-2 molecules and fragments thereof". Yet the instant specification does not provide sufficient guidance and direction how to make and use the scope of "B7-2 molecules and fragments thereof" by relying on limited sequences or homologous sequences, as encompassed by the claims.

Since the amino acid sequence of a polypeptide determines its structural and functional properties, predictability of which changes can be tolerated in a polypeptide's amino acid sequence and still retain similar functionality (e.g. B7-2 biological activity) requires a knowledge of and guidance with regard to which amino acids in the polypeptide's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which a polypeptide's structure relates to its functional usefulness. However, the problem of predicting polypeptide structure from mere sequence data of a limited number of amino acid and encoding nucleic acid sequences and, in turn, utilizing predicted structural determinations to ascertain binding or functional aspects of ligands and receptors (e.g., "B7-2 molecules") and finally what changes can be tolerated with respect thereto is complex and well outside the realm of routine experimentation. In re Fisher, 166 USPQ 18 indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

Because of the lack of sufficient guidance and predictability in determining which structures would lead to "B7-2 molecules and fragments thereof having the ability to costimulate a T cell and the ability to bind a CD28 or CTLA4", other than those disclosed in the specification as-filed with the desired properties and that the relationship between the sequence of a nucleic acid encoding a functional costimulatory molecule structure as the relationship between structure-function was not well understood and was not predictable. It would require an undue amount of experimentation for one of skill in the art to arrive at the breadth of "B7-2 molecules and fragments thereof", as broadly encompassed by the claimed invention.

In the absence of sufficient guidance and direction to the structural and functional analysis, the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue to make and use "B7-2 molecules and fragments thereof having the ability to costimulate a T cell and the ability to bind a CD28 or CTLA4" based upon limited sequences and homologous sequences, other than relying on those murine and human "B7-2 molecules", as disclosed in the specification as-filed.

"It is not sufficient to define the recombinant molecule by its principal biological activity, e.g. having protein A activity, because an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property." Colbert v. Lofdahl, 21 USPQ2d, 1068, 1071 (BPAI 1992).

A patent is granted for a completed invention, not the general suggestion of an idea and how that idea might be developed into the claimed invention. In the decision of Genentech, Inc, v. Novo Nordisk, 42 USPQ 2d 100,(CAFC 1997), the court held that:
"[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable" and that "[t]ossing out the mere germ of an idea does not constitute enabling disclosure". The court further stated that "when there is no disclosure of any specific starting material or of any of the conditions under which a process is to be carried out, undue experimentation is required; there is a failure to meet the enablement requirements that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art", "[I]t is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement".

Without sufficient guidance, making and using "B7-2 molecules and fragments thereof having the ability to costimulate a T cell and the ability to bind a CD28 or CTLA4" other than limiting the disclosed murine and human "B7-2 molecules" in the specification as-filed as would have been unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue.

Applicant's arguments have not been found persuasive.

Applicant is invited to limit the invention to the disclosed human and mouse "B7-2 molecules" to obviate this rejection.

8. Claims 1-14 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-25 of U.S. Patent No. 6,723,705.

Although the claims are not exactly the same, the recitation of "ex vivo" in the instant claims is encompassed by the patented claims and was either anticipated, immediately envisaged or an obvious variant of expressing B7-2 in tumor cells by direct injection of a nucleic acid encoding B7-2 into a tumor cell in order to increase the immunogenicity of tumor cells at the time the invention was made to one of ordinary skill.

Applicant's amendment, filed 08/018/2008, indicated that filing a terminal disclaimer will be considered when allowable subject matter is indicated.

9. New Grounds of Rejection

Claims 1-14 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable claims 1-12 of U.S. Patent No. 6,451,305 (Boussiotis et al.).

Although the claims are not exactly the same, the patented claims anticipate or render obvious the instant claims. The prior art modification of tumor cells with B7-2 anticipates the instant B7-2 molecules. The instant tumors encompassing carcinoma, sarcoma, melanoma and neuroblastoma would be obvious targeted tumors, given the claims of Boussiotis et al. to stimulate T cells via modifying tumors with costimulatory molecules such as B7-2 at the time the invention was made by the ordinary artisan.

10. Claims 1-14 are directed to an invention not patentably distinct from claims 1-12 of commonly assigned U.S. Patent No. 6,451,305 (Boussiotis et al.) for the reasons above in Section 9.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP Chapter 2300). Commonly assigned U.S. Patent No., discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications pending on or after December 10, 2004.

11. No claim is allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (571) 272-0844. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Eileen O'Hara can be reached on (571) 272-0878.

The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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